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(FILE 'HOME' ENTERED AT 17:04:49 ON 10 JUN 2003)

FILE 'CAPLUS' ENTERED AT 17:04:58 ON 10 JUN 2003

L1 1 S WO9806690/PN

SELECT L1 1 RN

L2 17 S E2-E15 OR E20-E23

=> save all

ENTER NAME OR (END):l10013971/l

L# LIST L1-L2 HAS BEEN SAVED AS 'L10013971/L'

=> save l2

ENTER NAME OR (END):a10013971/a

ANSWER SET L2 HAS BEEN SAVED AS 'A10013971/A'

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FILE 'CAPLUS' ENTERED AT 17:04:58 ON 10 JUN 2003

L1 1 S WO9806690/PN
SELECT L1 1 RN
L2 17 S E2-E15 OR E20-E23

=> save all

ENTER NAME OR (END):l10013971/l

L# LIST L1-L2 HAS BEEN SAVED AS 'L10013971/L'

=> save l2

ENTER NAME OR (END):a10013971/a

ANSWER SET L2 HAS BEEN SAVED AS 'A10013971/A'

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L1 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS
RN 50-36-2
RN 57-27-2
RN 64-17-5
RN 561-27-3
RN 19340-88-6P
RN 42042-64-8P
RN 57054-98-5P
RN 58869-18-4P
RN 58869-19-5P
RN 58869-28-6P
RN 202401-93-2P
RN 202401-94-3P
RN 202401-95-4P
RN 202401-96-5P
RN 202401-97-6P
RN 202401-98-7P
RN 202401-99-8P
RN 202402-00-4P
RN 202402-01-5P
RN 202402-02-6P
RN 202402-03-7P
RN 202402-04-8P
RN 202472-37-5P
RN 7664-93-9
RN 12125-02-9
RN 75-04-7
RN 96-48-0

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E1 1 12125-02-9/BI
E2 1 19340-88-6/BI
E3 1 202401-93-2/BI
E4 1 202401-94-3/BI
E5 1 202401-95-4/BI
E6 1 202401-96-5/BI
E7 1 202401-97-6/BI
E8 1 202401-98-7/BI
E9 1 202401-99-8/BI
E10 1 202402-00-4/BI
E11 1 202402-01-5/BI
E12 1 202402-02-6/BI
E13 1 202402-03-7/BI
E14 1 202402-04-8/BI
E15 1 202472-37-5/BI
E16 1 42042-64-8/BI
E17 1 50-36-2/BI

E18	1	561-27-3/BI
E19	1	57-27-2/BI
E20	1	57054-98-5/BI
E21	1	58869-18-4/BI
E22	1	58869-19-5/BI
E23	1	58869-28-6/BI
E24	1	64-17-5/BI
E25	1	75-04-7/BI
E26	1	7664-93-9/BI
E27	1	96-48-0/BI

L14 ANSWER 2 OF 3 USPATFULL on STN

SUMM Vitamin B2, also called **riboflavin**, is essential for humans and animals. Vitamin B2 deficiency is associated with inflammations of the mucous membranes of the mouth and throat, **itching** and inflammations in the skin folds and similar cutaneous lesions, conjunctival inflammations, reduced visual accuracy and clouding of the cornea. Babies and children may experience cessation of growth and loss of weight. Vitamin B2 therefore has economic importance, especially as vitamin supplement in cases of vitamin deficiency and as supplement to animal feed. It is also employed for coloring foodstuffs, for example in mayonnaise, icecream, blanchmange etc.

ACCESSION NUMBER: 2002:116040 USPATFULL
TITLE: Genes of purine biosynthesis from Ashbya gossypii and the use thereof in microbial riboflavin synthesis
INVENTOR(S): Pompejus, Markus, Waldsee, GERMANY, FEDERAL REPUBLIC OF
Seulberger, Harald, Neuhofen, GERMANY, FEDERAL REPUBLIC OF
Hoffken, Hans Wolfgang, Ludwigshafen, GERMANY, FEDERAL REPUBLIC OF
Revuelta Doval, Jose Luis, Salamanca, SPAIN
Jimenez, Alberto, Salamanca, SPAIN
Santos Garcia, Maria Angeles, Salamanco, SPAIN
PATENT ASSIGNEE(S): BASF Aktiengesellschaft, Ludwigshafen, GERMANY, FEDERAL REPUBLIC OF (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6391603	B1	20020521
APPLICATION INFO.:	US 1998-212247		19981216 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	DE 1997-19757755	19971223
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Achutamurthy, Ponnathapu	
ASSISTANT EXAMINER:	Steadman, David J.	
LEGAL REPRESENTATIVE:	Keil & Weinkauff	
NUMBER OF CLAIMS:	2	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	2 Drawing Figure(s); 2 Drawing Page(s)	
LINE COUNT:	625	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L14 ANSWER 3 OF 3 USPATFULL on STN

SUMM Vitamin B.sub.2, also termed **riboflavin**, is essential for humans and animals. Vitamin B.sub.2 deficiency results in inflammation of the mucous membranes of the mouth and throat, cracks in the corners of the mouth, **itching** and inflammation in skin folds and similar skin damage, conjunctivitis, diminished visual acuity and clouding of the cornea. Cessation of growth and decrease in weight can occur in babies and children. Vitamin B.sub.2 is therefore of particular economic importance as a vitamin preparation for use in vitamin deficiency and as a feed additive. In addition, it is also employed as a food dye, for example in mayonnaise, ice cream, desserts such as blanchmange, etc.

ACCESSION NUMBER: 1999:136993 USPATFULL
TITLE: Riboflavin-production process by means of micro-organisms with modified isocitratlyase activity
INVENTOR(S): Kasler, Bruno, Ludwigshafen, Germany, Federal Republic of

Sahm, Hermann, Julich, Germany, Federal Republic of
 Stahmann, Klaus-Peter, Julich, Germany, Federal
 Republic of
 Schmidt, Georg, Aldenhoven, Germany, Federal Republic
 of
 Boddecker, Theo, Julich, Germany, Federal Republic of
 Seulberger, Harald, Dossenheim, Germany, Federal
 Republic of
 PATENT ASSIGNEE(S): BASF Aktiengesellschaft, Ludwigshafen, Germany, Federal
 Republic of (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5976844		19991102
	WO 9703208		19970130
APPLICATION INFO.:	US 1998-981690		19980501 (8)
	WO 1996-EP3009		19960710
			19980501 PCT 371 date
			19980501 PCT 102(e) date

	NUMBER	DATE
PRIORITY INFORMATION:	DE 1995-19525281	19950713
	DE 1995-19545468	19951205
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	Granted	
PRIMARY EXAMINER:	Wax, Robert A.	
ASSISTANT EXAMINER:	Mayhew, Bradley S.	
LEGAL REPRESENTATIVE:	Keil & Weinkauff	
NUMBER OF CLAIMS:	11	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	10 Drawing Figure(s); 8 Drawing Page(s)	
LINE COUNT:	663	
CAS INDEXING IS AVAILABLE FOR THIS PATENT.		

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L3 ANSWER 1 OF 1 USPATFULL on STN

AB Compositions for skin treatment are disclosed and include **nicotinamide**, **nicotinic acid**, and **nicotinic esters** as active ingredients. The compositions are applied topically to the skin to treat skin conditions including **acne**, fine lines and age spots, **itching** and pain from insect bites, bee stings, fungi (including athlete's foot and jock itch), flaking and/or scaly skin (including dandruff, seborrheic **dermatitis**, psoriasis and heat rash), and burns. Different compositions are presented for use as an **acne** treatment, a face and body wash, a dermatophyte (nail fungus) treatment. Still another is intended for use in makeup, and another in lipstick.

SUMM The present invention relates generally to compositions for treating various skin conditions and, more particularly to a topically applied skin treatment composition including a **nicotinic ester** as an active ingredient.

SUMM Various compositions containing **nicotinic esters** have been known and commonly used for inducing and stimulating hair growth. Examples of these can be found in the U.S. patents to Grollier, U.S. Pat. Nos. 5,157,036 and 4,968,685. In U.S. Pat. No. 5,468,492, Szaloki discloses a use of vitamin E **nicotinate** as a rubefacient to improve the circulation of the blood of the scalp. Other compositions containing methyl **nicotinate** have been proposed as an analgesic for the symptomatic relief of localized pain of musculo-skeletal etiology, as evidenced by the U.S. patent to Fisher, U.S. Pat. No. 3,880,996.

SUMM A product is available and sold under the trade name FINALGON, which is a topical rubefacient including **nicotinic acid**. The product is intended for use as a temporary relief from pain caused by muscular rheumatism and does not disclose use as a skin treatment.

SUMM A variety of published articles describe the effects and uses of **nicotinic acid**, **nicotinamide** and methyl **nicotinate** (Murrell, T., "The Cutaneous Reaction to **Nicotinic Acid**," A.M.A. Archives of Dermatology, 79:545-552, May, 1959, Shalita, A. R., "Topical **nicotinamide** compared with clindamycin gel in the treatment of inflammatory **acne vulgaris**," International Journal of Dermatology, 34(6): 434-7, June, 1995, and Remme, J. J., "Bullous pemphigoid successfully controlled by tetracycline and **nicotinamide**," British Journal of Dermatology, 133(1): 88-90, July, 1995). None of these articles describe a use of the particular compositions of **nicotinamide**, its derivatives, **nicotinic acid**, its esters, or their derivatives as presented by this invention.

SUMM In U.S. Pat. Nos. 3,729,685 and 3,906,108 Kligman and Felty, respectively, describe a method of **acne** treatment which involves topical application of vitamin A to the skin. This method does not, however, include the use of vitamin B3, **nicotinic acid** or any salt thereof for **acne** treatment. One disadvantage of using vitamin A in skin treatment is the substantial skin irritation vitamin A causes. This irritation makes such treatment unpleasant and may even lead to an individual foregoing treatment altogether. Although a cream formulation of vitamin A may reduce the undesirable side effects, it does not do so entirely. This leaves an individual who applies the vitamin A treatment with irritated, stinging and itching skin.

SUMM The prior art does not provide for the topical application of **nicotinamide**, its derivatives, **nicotinic acid**, and **nicotinic esters** or their derivatives in the compositions presented herein. The present invention presents a spectrum of unique

and novel formulas by which **nicotinamides**, **nicotinic acids** and **nicotinic esters** may be topically applied to the skin. Some of the formulas embody an original compilation of ingredients which include skin moisturizers, emollients, vitamin E, carriers and other beneficial elements. Some formulas are designed to dry quickly and clearly upon application. These formulas provide the user with a smooth and even skin tone without the greasy, sticky finish or irritation caused by many other skin care products. Further, these formulas are effective in treating a variety of disorders and skin conditions, including the removal of blackheads.

SUMM The present invention relates to a discovery that a **nicotinic ester** and particularly the compound methyl **nicotinate**, is highly beneficial when topically applied to treat skin conditions. More particularly, when combined with a skin moisturizer, a suitable carrier, an emollient (e.g. glycerol or glycerin), vitamin E and other elements and excipients, methyl **nicotinate**, and **nicotinic acid** have surprising efficacy in treating various skin conditions including: **acne** blemishes; **acne** pimples, blackheads and whiteheads; psoriasis; seborrheic dermatitis, or dandruff; large pores, fine lines and age spots; stretch marks; cellulite; itching; pain and itching from insect bites and stings; fungi; varicose veins; flaking and scaly skin; burns (including sunburn); bedsores and black and blue marks.

DETD In the following preferred embodiments, the active ingredient listed is methyl **nicotinate**. The composition might otherwise utilize **nicotinamides**, derivatives thereof, **nicotinic acids**, **nicotinic esters** or derivatives thereof as an active ingredient.

DETD In a preferred embodiment intended to treat **acne**, psoriasis, seborrheic dermatitis or dandruff and dermatophyte fungi, the composition has the following ingredients:

DETD	Methyl nicotinate	0.01 to 1%
	Niacin	0.01 to 1%
	Glycolic Acid	0.01 to 20%
	Aloe vera gel	35 to 45%
	Glycerin	0.8 to 1.8%
	DMDM hydantoin	0.02 to 0.25%
	Tetrasodium EDTA	0.05 to 0.15%
	Vitamin E	0.01 to 0.1%
	Polysorbate-20	0.5 to 1.0%
	Silk amino acids	0.01 to 0.1%
	Hydrolyzed collagen	0.01 to 0.1%

DETD The preferred method of using the composition for **acne**, psoriasis, dermatitis or dandruff and dermatophyte fungi is to apply it directly to the skin or other affected area without the glycolic acid. To promote vasodilation, this may be done using the palm of the hands or an applicator such as a cotton or a cosmetic pad. The same composition with glycolic acid is then applied on top of the first composition as a spot treatment on the firm elevation of the pimple or whitehead, dead skin of psoriasis and fungi where bacteria breeds. It is applied twice a day for 2 to 3 days to the affected area. The glycolic acid in the second composition acts as an exfoliant, and it peels away the unwanted material. It is removed to stop the peeling, and the first composition is applied to continue vasodilation to improve the supply of blood to the affected cells.

DETD Persons using the composition have reported the clearing up of any blemishes as well as an inhibitory effect wherein new blemishes or breakouts are prevented from forming. The composition's users relate marked improvements in their skin's texture and **acne** condition, psoriasis and fungus. Other users have stated that the product improved their **acne** condition as well as the general color and clarity of their skin within a relatively short period of use,

two days.

DETD	Methyl nicotinate	0.01 to 20%
	Niacin	0.01 to 1%
	Aloe vera gel	60 to 70%
	Ammonium lauryl sulfate	20 to 28%
	Cocamidopropyl betaine	3 to 5%
	Lauramide DEA	3 to 5%
	Glycerin	0.8 to 2.5%
	Methylparaben	0.8 to 1.2%
	Propylparaben	0.8 to 1.2%
	Propylene glycol	0.8 to 1.2%
	Imidazolidinyl urea	0.8 to 1.2%
	Guanine	0.1 to 0.15%
	Tea-lauryl sulfate	0.1 to 0.15%
	Isopropyl alcohol	0.1 to 0.15%
	Methylcellulose	0.1 to 0.15%
	Vitamin E	0.01 to 0.1%
	Silk amino acids	0.01 to 0.1%
	Hydrolyzed collagen	0.01 to 0.1%
	Chamomile	0.01 to 0.1%

DETD Persons using this composition have reported that it has kept their face from getting oily, prevented breakouts, and reduces fine lines on the face. The composition is said to leave a tingling sensation with increased warmth and has been very useful in treatment of itching sensations caused by rashes and insect bites. The composition stimulates the oil glands dissipating the oil so blood can get to the cells. The composition is also useful in treating other skin conditions such as psoriasis, athlete's foot, **eczema**, hives or other allergic reactions and associated symptoms that accompany these conditions such as itching. The composition removes dead skin and penetrates the pores.

DETD	Methyl nicotinate	0.01 to 8%
	Niacin	0.01 to 1%
	Glycerin	0.8 to 2.5%
	Isopropyl palmitate	1 to 15%
	Myristyl myristate	1 to 15%
	Glyceryl ricinoleate	1 to 15%
	Octyldodecanol	1 to 15%
	Microcrystalline wax	1 to 10%
	Acetylated lanolin	1 to 10%
	Candelilla wax	1 to 10%
	Carnauba	1 to 10%
	Isopropyl lanolate	1 to 15%
	Cetyl alcohol	1 to 15%
	Mineral oil	1 to 15%.

DETD	Methyl nicotinate	0.01 to 8%
	Niacin	0.01 to 1%
	Glycerin	0.8 to 2.5%
	Octylmethoxycinnamate	0.8 to 2%
	Benzophenone-3	0.8 to 2%
	Propylene glycol	0.8 to 2%
	Soy lecithin	0.08 to 2%
	Glyceryl stearate	0.08 to 2%
	Peg-100 stearate	0.08 to 2%
	Cetearyl alcohol	0.1 to .15%
	Ceteareth-20	0.08 to 2%
	Sodium PCA	1 to 10%
	Tocopheryl linoleate	1 to 10%
	Tocopheryl acetate	1 to 10%
	Methylparaben	0.8 to 2%
	Ethylparaben	0.8 to 2%
	Propylparaben	0.8 to 2%
	DMDM hydantoin	0.8 to 2%

CLM What is claimed is:

1. A method of treating psoriasis affected areas of the skin comprising: topically applying to said affected areas twice a day an effective amount of a composition comprising by weight, 0.01 to 1.0% methyl **nicotinate**; by weight, **niacin** 0.01 to 1%; by weight, 35 to 45% aloe vera gel; by weight, 0.8 to 1.8% glycerin; by weight, 0.02 to 0.25% DMDM hydantoin; by weight, 0.05 to 0.15% tetrasodium EDTA; by weight, 0.01 to 0.1% Vitamin E by weight, 0.5 to 1.0% polysorbate-20; by weight, 0.01 to 0.1% silk amino acids; by weight, 0.01 to 0.1% hydrolyzed collagen; and, water.

2. A method of treating psoriasis affected areas of the skin comprising: topically applying to said affected areas twice a day for two to three days an effective amount of a composition comprising by weight, 0.01 to 1.0% methyl **nicotinate**; by weight, **niacin** 0.01 to 1%; by weight 35 to 45% aloe vera gel; by weight, 0.8 to 1.8% glycerin; by weight, 0.02 to 0.25% DMDM hydantoin; by weight, 0.05 to 0.15% tetrasodium EDTA; by weight, 0.01 to 0.1% Vitamin E by weight, 0.5 to 1.0% polysorbate-20; by weight, 0.01 to 0.1% silk amino acids; by weight, 0.01 to 0.1% hydrolyzed collagen; by weight, 0.01 to 20% of a peeling agent, glycolic acid; and, water.

ACCESSION NUMBER: 2001:93529 USPATFULL
 TITLE: Composition for treating skin conditions
 INVENTOR(S): Scivoletto, RoseMarie, 10249 El Paraiso Pl., Delray
 Beach, FL, United States 33446

	NUMBER	KIND	DATE
	-----	-----	-----
PATENT INFORMATION:	US 6248763	B1	20010619
APPLICATION INFO.:	US 1999-414849		19991012 (9)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1998-82292, filed on 19 May 1998		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	GRANTED		
PRIMARY EXAMINER:	Cook, Rebecca		
LEGAL REPRESENTATIVE:	Oltman, Flynn & Kubler		
NUMBER OF CLAIMS:	2		
EXEMPLARY CLAIM:	1		
LINE COUNT:	282		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=>

Kim, Vickie

From: Kim, Vickie
Sent: Friday, June 06, 2003 4:34 PM
To: 'ctweigell@bryancave.com'
Subject: RE: 10/009225

Hi, Mr. Weigell.
Here's my proposal.

8. (once amended) A method for the treatment of pruritus in a subject in need of the same, wherein the method comprises systemically administering to the said subject a composition consisting essentially of a combination of an effective amount of nicotinic acid or nicotinamide and riboflavin, optionally in a pharmaceutically acceptable vehicle or carrier suitable for systemic administration, and excluding any other vitamin agent and any other inflammatory agent besides said nicotinic acid or said riboflavin.
9. (once amended) The method according to claim 8, wherein said pruritus is uremic pruritus associated with renal insufficiency.
10. (once amended) The method according to claim 8, wherein said pruritus is chosen from the group consisting of senile pruritus that is itching of aged skin, vulvar pruritus, scrotal pruritus and anal pruritus.
26. (one amended) The method according to claim 8, wherein said same.....
27. OK
28. OK

Cancel claims 1-7, 11-25, 29-30.

This proposal is made based on the several relevant prior art teaching synergism between nicotinic acid and riboflavin, and the intended use for each component, possible combination therapy for dermatitis and inflammations, etc.
If this proposal is not acceted, The supplemental election requirement will be issued because pruritis treatment(tx) and treatment of non-infective, non-neoplastic, non-rheumatic disorders involving itching and/or inflammation is materially different and search required for pruritus is not same for the said disorders and is not anticipating for other species. By reviewing numerous references which support lack of unity between these said species and thus, election requirement deems to be proper and
it is believe to be that issuance of further election requirement is necessary for the accurate examination.

I like to accept any counter offer that contains minor changes as long as they do not change the allowable subject matter that I proposed.

Looking forward to hear from you.

Vickie Kim
Art Unit 1614
(703) 305-1675

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pruritis

Itching. Pruritis can result from drug reaction, food allergy, kidney or liver disease, cancers, parasites, aging or dry skin, contact skin reaction, such as poison ivy, and for unknown reasons.

(12 Dec 1998)

Previous: [prurigo infantilis](#), [prurigo mitis](#), [prurigo nodularis](#), [prurigo simplex](#), [pruritic](#)

Next: [pruritus](#), [pruritus aestivalis](#), [pruritus ani](#), [pruritus balnea](#)

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pruritus

1. <symptom> Itching, an unpleasant cutaneous sensation that provokes the desire to rub or scratch the skin to obtain relief.
2. Any of various conditions marked by itching, the specific site or type being indicated by a modifying term.

Origin: L. From prurire = to itch

(06 Oct 1997)

Previous: prurigo mitis, prurigo nodularis, prurigo simplex, pruritic, pruritis

Next: pruritus aestivalis, pruritus ani, pruritus balnea, pruritus hiemalis

L11 ANSWER 1 OF 4 USPATFULL

AB A dietary supplement is disclosed which supplies the skeletal muscle with energy and protects the cardiovascular tract, the characterising components of which comprise propionyl L-carnitine, coenzyme Q.sub.10, **nicotinamide**, **riboflavin** and pantothenic acid.

ACCESSION NUMBER: 2003:3057 USPATFULL
 TITLE: Dietary supplement energy-providing to skeletal muscles and protecting the cardiovascular tract
 INVENTOR(S): Gaetani, Franco, Roma, ITALY

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003003091	A1	20030102
APPLICATION INFO.:	US 2001-980278	A1	20011203 (9)
	WO 2001-IT167		20010330

	NUMBER	DATE
PRIORITY INFORMATION:	IT 2000-RM2000000016520000404	
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	Nixon & Vanderhye, 1100 North Glebe Road 8th Floor, Arlington, VA, 22201-4714	
NUMBER OF CLAIMS:	8	
EXEMPLARY CLAIM:	1	
LINE COUNT:	468	

L11 ANSWER 2 OF 4 USPATFULL

AB Vitamin and mineral absorption in warm-blooded animals is promoted by means of a class of vitamin chelates where at least one of the bonds between the metal ion and the vitamin ligand is formed between the ion and an electron rich .pi.-cloud of an aromatic ring of the water soluble vitamin. The chelate, containing a total of from one to three ligands, may contain from one up to three vitamin ligands which form a .pi.-bond with the mineral and, when present, one or two amino acid, dipeptide or tripeptide ligands. The mineral is selected from the group consisting of Fe, Cu, Zn, Mg, Mn and Ca. The water soluble vitamin ligand is preferably a residue of **nicotinamide**, **nicotinic** acid, pyridoxine, thiamine, **riboflavin** and folic acid. The amino acid may be any of the naturally occurring .alpha.-amino acids such as glycine. The .pi.-bond vitamin chelates are absorbed more readily from both the gastric and intestinal areas of the GI tract than vitamins or minerals administered separately or as mixtures.

ACCESSION NUMBER: 94:20164 USPATFULL
 TITLE: II-bond aromatic vitamin chelates
 INVENTOR(S): Ashmead, Harvey H., Kaysville, UT, United States
 PATENT ASSIGNEE(S): Albion International, Inc., Clearfield, UT, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5292729		19940308
APPLICATION INFO.:	US 1992-930747		19920814 (7)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Shah, Mukund J.		
ASSISTANT EXAMINER:	Sripada, P. K.		
LEGAL REPRESENTATIVE:	Thorpe, North & Western		
NUMBER OF CLAIMS:	50		
EXEMPLARY CLAIM:	1		
LINE COUNT:	976		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 3 OF 4 USPATFULL

AB In paticular, the medium also contains in part per million about: 3.0 H.sub.3 BO.sub.3, 10.0 MnSO.sub.4.H.sub.2 O, 6.0 ZnSO.sub.4.7H.sub.2 O, 0.25 Na.sub.2 MoO.sub.4.2H.sub.2 O, 0.025 CuSO.sub.4.5H.sub.2 O, 0.025 CaCl.sub.2.6H.sub.2 O, 0.75 KI, 2.5 **Nicotinic** acid, 10.0 Thiamine HCl, 1.0 Pyridoxine HCl, 100.0 M-inositol, 0.5 Glycine, 0.5 Folic acid, 0.05 Biotin, 0.5 D-Ca-Pantothenate, 0.25 **Riboflavin**, 0.5 Ascorbic acid, 0.1 choline chloride, 1.0 L-cysteine HCl, 10.0 Malic acid and 50.0 Casein Hydrolysate. Furthermore, the medium desirably contains about 3 percent sucrose or glucose.

ACCESSION NUMBER: 84:54076 USPATFULL
TITLE: Process and nutrient medium for micropropagation of cassava
INVENTOR(S): Tang, Archie F., Redwood City, CA, United States
PATENT ASSIGNEE(S): International Plant Research Institute, San Carlos, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4473648		19840925
APPLICATION INFO.:	US 1982-378420		19820514 (6)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Wiseman, Thomas		
ASSISTANT EXAMINER:	Tarcza, John E.		
LEGAL REPRESENTATIVE:	White, John P.		
NUMBER OF CLAIMS:	4		
EXEMPLARY CLAIM:	1		
LINE COUNT:	368		

L11 ANSWER 4 OF 4 USPATFULL

AB A dietary supplement, for use with from 61.3 to 123 grams of dried skimmed milk (or the equivalent quantity of liquid skimmed milk) in the dietary regime disclosed in copending Application Serial No. 338,257 (U.S. Pat. No. 4,009,265), in which the amount of said supplement which contains a datum level of 18.+-.9 mg iron also contains at least 182 mg sodium, at least 308 mg potassium and at least 64 mg magnesium, as well as Vitamin A in an amount of at least 750 .mu.g retinol equivalents, at least 100 i.u. Vitamin D, at least 0.76 mg thiamine, at least 14 mg **nicotinic** acid (or **nicotinamide**), and at least 18 mg ascorbic acid, and in which the total calorie content (if any) of that amount of supplement is not greater than 200 Kcals, usually is less than 100 Kcalories, and preferably does not exceed 25 Kcalories. The supplement preferably also contains 50-150 .mu.g iodine and/or at least 157 mg phosphorus, and/or traces of copper, zinc and manganese, and/or at least 2 mg Vitamin B.sub.6, at least 5 .mu.g Vitamin B.sub.12, at least 30 i.u. Vitamin E, at least 0.4 mg folic acid and at least 0.7 mg **riboflavin**. It also desirably contains trace amounts of pantothenic acid, d-biotin, p-aminoenzoic acid, choline and/or Vitamin K, as well as optionally up to 500 mg of L-methionine and/or L-cysteine and/or L-cystine, and/or from 1.0 g to 10 g of essential fatty acid(s).

ACCESSION NUMBER: 80:60402 USPATFULL
TITLE: Dietary supplement and dietary methods employing said supplement for the treatment of obesity
INVENTOR(S): Howard, Alan N., 10 Topcliffe Way, Cambridge, England

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4237118		19801202
APPLICATION INFO.:	US 1976-686594		19760514 (5)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1973-338257, filed on 5 Mar 1973, now patented, Pat. No. US 4009265		

	NUMBER	DATE
PRIORITY INFORMATION:	GB 1972-10439	19720306
	GB 1975-21029	19750516
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	Granted	
PRIMARY EXAMINER:	Roberts, Elbert L.	
LEGAL REPRESENTATIVE:	Barron, Alexis	
NUMBER OF CLAIMS:	30	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	1 Drawing Figure(s); 1 Drawing Page(s)	
LINE COUNT:	1002	
CAS INDEXING IS AVAILABLE FOR THIS PATENT.		

=> d 116 1-3 hit, ibib

L16 ANSWER 1 OF 3 USPATFULL

SUMM When the Gram-positive bacilli are reduced or disappear in vagina, vaginal pH value rises and disturbance of vaginal bacterial flora results from abnormal increases of Gram-negative bacilli, Gram-positive cocci and Gram-negative cocci, which can cause harm to the human body and lead to a range of diseases. The most typical condition resulting from altered vaginal flora is bacterial vaginosis (BV). BV is characterized by the reduction or even disappearance of Lactobacillus and other Gram-positive bacilli in the vagina, accompanied by decreased acidity (pH value>4.6) in the vagina, and abnormal increases of such bacteria as Gram-negative bacilli including Gardnerella, Bacteroides and motile-curved bacilli; Gram-negative cocci such as Veillonella; and Gram-positive cocci such as Streptococcus. Such changes in the bacterial flora can cause vaginal secretions to exhibit an unpleasant odor, and may be associated with **pruritus** of vulva, and symptoms. In addition, BV may also be related to IUGR [1], PTL, PROM [2], abortion, and obstetric infections such as chorio-amnionitis, puerperal endometritis, vaginal wall phlegmon after hysterectomy, female upper genital tract infection (salpingitis), and urinary infection, etc. [3]. A high rate of morbidity is associated with vaginal bacterial flora disturbance. According to one report, about 45% or more vaginitis cases result from disturbance of vaginal bacterial flora [3], and 4-15% of American female students in universities suffer from bacterial vaginosis [4], which has led to serious compromise to health and quality of life.

DETD Ms. Jiang, female, aged 30. The vaginal secretions of hers had exhibited unpleasant fish-odor, accompanying **pruritus** of vulvae for 2 years. After having born a child two years ago this patient had begun suffering from the increased quantity of vaginal secretions, which had exhibited unpleasant fish-odor especially after intercourse, and from **pruritus** of the vulvae which was so severe sometimes that she could not fall asleep. Having been tested and reported "neuplasma positive" in one hospital, she had been treated with several antibiotics which could relieve her symptoms temporarily. But the symptoms usually relapsed after the menstruation. She had also used various vaginal douches, and the symptoms relieved temporarily and then relapsed after stopping treatments. The present inventor found that there were a great mass of bacteria in Gram smears of the vaginal secretions of the patient and most of them were Gram negative bacilli and Gram negative cocci, there was few Gram positive bacilli and a few of white blood cells. The pH values of the vaginal secretions of this patient was 5.4. Diagnosed as "bacterial vaginosis" by the present inventor, this patient was treated with the composition of this invention, which contained 12% (W/V) of lactose and the pH value was 5.0. The drug was intravaginally administered, 3 ml for each time, once a day. After the treatment continued successively for three days, the symptoms of the patient relieved significantly and the pH value of the vaginal secretions

decreased to 4.6. The Gram smears showed a lot of Gram-negative bacilli, Gram negative cocci, but the quantity of Gram positive cocci increased and many of Gram positive bacilli appeared.

DETD

Fructooligosaccharide 14.0% (W/V)
Histidine 100 ppm
Methionine 50.0 ppm
Riboflavin 0.2 ppm
Thiamine 0.2 ppm
Nicotinic acid 0.2 ppm
Calcium pantothenate 0.2 ppm
Xanthan gum 1.8% (W/V)
Distilled water q.s.
pH 5.5

DETD

Dextrin 10.0% (W/V)
Glucose 2.0% (W/V)
Histidine 100 ppm
Methionine 50.0 ppm
Riboflavin 0.2 ppm
Thiamine 0.2 ppm
Nicotinic acid 0.2 ppm
Calcium pantothenate 0.2 ppm
Xanthan gum 1.0% (W/V)
pH 6.0

ACCESSION NUMBER: 2002:217253 USPATFULL
TITLE: Method for promoting the growth of gram-positive bacilli and increasing the acidity in vagina
INVENTOR(S): Zeng, Zhongming, Shenzhen, CHINA
PATENT ASSIGNEE(S): Shanghai Jiao Da Onlly Co., Ltd., Shanghai, CHINA (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6440949	B1	20020827
APPLICATION INFO.:	US 2000-578177		20000524 (9)
RELATED APPLN. INFO.:	Continuation of Ser. No. WO 1998-CN278, filed on 24 Nov 1998		

	NUMBER	DATE
PRIORITY INFORMATION:	CN 1997-1227	19971124
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Fonda, Kathleen K.	
ASSISTANT EXAMINER:	Maier, Leigh C.	
LEGAL REPRESENTATIVE:	Darby & Darby	
NUMBER OF CLAIMS:	8	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	0 Drawing Figure(s); 0 Drawing Page(s)	
LINE COUNT:	1062	
CAS INDEXING IS AVAILABLE FOR THIS PATENT.		

L16 ANSWER 2 OF 3 USPATFULL

SUMM A systemic vitamin A derivative for the treatment of nodular acne, known as isotretinoin, is commercially available under the name ACCUTANE.RTM., from Roche Laboratories in Nutley, N.J. It has been found that treatment using isotretinoin can clear up as much as 85 percent of the acne over a 4 to 6 month period. [Id.]. Also, the patient's condition tends to improve even after the treatment has ceased. Unfortunately, side effects often result from treatment using isotretinoin, and patients need to be monitored carefully. Monthly testing of the patient's liver, lipids and

glucose is necessary to monitor the response to isotretinoin. The side effects are often mucocutaneous: cheilitis (dry, blistering lips), dry eyes or nose, eye irritation, **pruritus**, epistaxis (nosebleed), mild alopecia (hair loss), and some photosensitivity. [Id.]. Furthermore, isotretinoin is teratogenic, and therefore poses a serious risk of causing birth defects in pregnant women. Birth defects such as craniofacial, cardiac, and central nervous system abnormalities may result from even small amounts of isotretinoin taken over short periods of time. Thus, doctors administering this treatment often require females to take effective contraception prior to, during, and after treatment. [Roche Laboratories Inc., Important Information Concerning Your Treatment with Accutane, 6th ed., (1996)].

SUMM The present invention also optionally includes several vitamin B sources. Vitamin B.sub.1, also commonly known as thiamine, aids carbohydrate metabolism, as well as the growth and maintenance of healthy skin. Both vitamin B.sub.2 and B.sub.3 are involved in tissue repair. Vitamin B.sub.2, also commonly known as **riboflavin**, is involved in both the protein and the liquid metabolism necessary to rebuild damaged skin tissues. Moreover, Vitamin B.sub.3 acts as a vasodilator, increasing the blood flow to the skin and other tissues. Vitamin B.sub.3 includes several vitamin B complexes, such as niacin, **nicotinic acid**, niacinamide, and **nicotinamide**. Preferably, niacinamide is used in the present invention. Vitamin B.sub.5 complex also aids in several metabolic functions. All of the above vitamin B complexes also enhance the effectiveness of vitamin B.sub.6 in treating the skin. Preferably, the B.sub.5 source is pantothenic acid. Each of these vitamin B complexes may be found in the present pharmaceutical composition in about 0.05 to 15 weight percent, preferably about 0.2 to 5 weight percent, and more preferably about 0.3 to 3 weight percent. A unit dose of the above vitamin B complexes is typically about 1 mg to 50 mg, preferably about 1.5 mg to 35 mg, and more preferably about 2 mg to 20 mg.

DETD

INGREDIENTS	MG PER PERCENT BY WEIGHT	CHEMICAL OR SCIENTIFIC NAME
Vitamin E Succinate (63.1%)	158.5	
	13.4%	D-alpha tocopheryl acid succinate
L-Lysine Hcl (80.0%)	13.2%	L-Lysine hydrochloride
Calcium Ascorbate (81.0%)	154.3	
	13.0%	Calcium ascorbate
Burdock Root	12.7%	150.0
		Arctium lappa
Yellow Dock	10.6%	125.0
		Rumex crispus polygonacae
L-Proline	10.6%	125.0
		L-Proline
Horsetail extract (Silica)	100.0	
	8.4%	Equisetrum arvense
Magnesium Oxide (60.0%)	7.0%	

		Magnesium oxide
Zinc Ascorbate (15.0%)	2.1%	
		Zinc ascorbate
Vitamin B.sub.6 (Pyridoxine HCL)	15.1	1.3%
		Pyridoxine hydrochloride
(82.7%)		
Grape Seed Extract	1.1%	5
		Proanthocyanidins
Vitamin B.sub.3 (Niacin)	12.5	
	1.1%	
		Niacinamide
Beta Carotene (yields 1,250	10.0	
	0.9%	
		Beta carotene
IU per tablet)		
Selenomethionine (0.5%)	0.8%	
		L-selenomethionine
Biotin (1.0%)	0.6%	7.5
		Biotin
Vitamin B.sub.5 (91.7%)	0.6%	
		Pantothenic Acid
Vitamin B.sub.2 (Riboflavin)	6.3	
	0.5%	
		Riboflavin
Vitamin B.sub.1 (Thiamine)	6.3	
	0.5%	
		Thiamine
CHROMEMATE CHROMIUM GTF .TM.	6.3	
	0.5%	
(0.2%)		Chromium polynicotinate
		Chromium organically bound
		to nicotinic acid (niacin,
		vitamin B.sub.3)
Vitamin A Palmitate (yields	2.5	
	0.2%	
		Vitamin A palmitate
1,250 IU per tablet)		
Chromium Picolinate (12.0%)	0.1	
	0.01%	
		Chromium picolinate

ACCESSION NUMBER:	1999:121419	USPATFULL
TITLE:	Pharmaceutical compositions and methods for treating	
	acne	
INVENTOR(S):	Murad, Howard, 4316 Marina City Dr., Marina del Rey,	
	CA, United States 90292	

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5962517		19991005
APPLICATION INFO.:	US 1998-16800		19980130 (9)

NUMBER	DATE
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L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN

RN 98-92-0 REGISTRY

CN 3-Pyridinecarboxamide (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Nicotinamide (8CI)

OTHER NAMES:

CN .beta.-Pyridinecarboxamide

CN 3-(Aminocarbonyl)pyridine

CN 3-Amidopyridine

CN 3-Carbamoylpyridine

CN 3-Pyridinecarboxylic acid amide

CN Aminicotin

CN Benicot

CN Delonin Amide

CN Dipegyl

CN m-(Aminocarbonyl)pyridine

CN NAM

CN Niacinamide

CN Niavit PP

CN Nicamina

CN Nicamindon

CN Nicasir

CN Nicobion

CN Nicofort

CN Nicosan 2

CN Nicosylamide

CN Nicotilamide

CN Nicotine acid amide

CN Nicotinic acid amide

CN Nicotinic amide

CN Nicotylamide

CN Nicovit

CN Nicovitina

CN Nictoamide

CN Niocinamide

CN Niozymin

CN NSC 13128

CN NSC 27452

CN Papulex

CN Pelmin

CN Pelmine

CN Pelonin amide

CN Vi-Nicotyl

CN Vitamin B

CN Vitamin B3

FS 3D CONCORD

DR 123574-63-0, 37321-14-5, 78731-47-2

MF C6 H6 N2 O

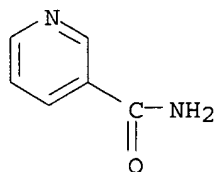
CI COM

LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DIOGENES, DRUGU, EMBASE, GMELIN*, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PDLCOM*, PHAR, PIRA, PROMT, RTECS*, SPECINFO, TOXCENTER, USAN, USPAT2, USPATFULL, VTB

(*File contains numerically searchable property data)

Other Sources: DSL**, EINECS**, TSCA**, WHO

(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

8103 REFERENCES IN FILE CA (1907 TO DATE)
273 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
8111 REFERENCES IN FILE CAPLUS (1907 TO DATE)
9 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN

RN 59-67-6 REGISTRY

CN 3-Pyridinecarboxylic acid (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Nicotinic acid (7CI, 8CI)

OTHER NAMES:

CN .beta.-Pyridinecarboxylic acid

CN 3-Carboxypyridine

CN 3-Carboxypyridine

CN 3-Pyridylcarboxylic acid

CN Akotin

CN Apelagrin

CN Daskil

CN Efacin

CN Enduracin

CN Linic

CN Niac

CN Niacin

CN Niacor

CN Niaspan

CN Nicacid

CN Nicangin

CN Nico-Span

CN Nicobid

CN Nicodelmine

CN Nicolar

CN Niconacid

CN Nicosan 3

CN Nicotinipca

CN Nicyl

CN NSC 169454

CN Nyclin

CN Pellagrin

CN Pelonin

CN Slo-niacin

CN SR 4390

CN Wampocap

FS 3D CONCORD

DR 123574-58-3

MF C6 H5 N O2

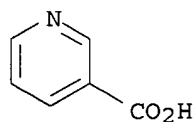
CI COM

LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*,
BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS,
CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM,
CSNB, DDFU, DETHERM*, DIOGENES, DIPPR*, DRUGU, EMBASE, GMELIN*, HODOC*,
HSDB*, IFICDB, IFIPAT, IFIUDB, IMSCOSEARCH, IPA, MEDLINE, MRCK*,
MSDS-OHS, NAPRALERT, NIOSHTIC, PDLCOM*, PHAR, PIRA, PROMT, RTECS*,
SPECINFO, SYNTHLINE, TOXCENTER, TULSA, ULIDAT, USAN, USPAT2, USPATFULL,
VETU, VTB

(*File contains numerically searchable property data)

Other Sources: DSL**, EINECS**, TSCA**, WHO

(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

14461 REFERENCES IN FILE CA (1907 TO DATE)
547 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
14481 REFERENCES IN FILE CAPLUS (1907 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

UMM The present invention relates to a discovery that a nicotinic ester and particularly the compound methyl nicotinate, is highly beneficial when topically applied to treat skin conditions. More particularly, when combined with a skin moisturizer, a suitable carrier, an emollient (e.g. glycerol or glycerin), vitamin E and other elements and excipients, methyl nicotinate, and **nicotinic** acid have surprising efficacy in treating various skin conditions including: acne blemishes; acne pimples, blackheads and whiteheads; psoriasis; seborrheic dermatitis, or dandruff; large pores, fine lines and age spots; stretch marks; cellulite; **itching**; pain and **itching** from insect bites and stings; fungi; varicose veins; flaking and scaly skin; burns (including sunburn); bedsores and black and blue marks.

PI US 6248763 B1 20010619

L7 ANSWER 13 OF 27 USPATFULL on STN

ACCESSION NUMBER: 2001:93529 USPATFULL

TITLE: Composition for treating skin conditions

INVENTOR(S): Scivoletto, RoseMarie, 10249 El Paraiso Pl., Delray
Beach, FL, United States 33446

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6248763	B1	20010619
APPLICATION INFO.:	US 1999-414849		19991012 (9)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1998-82292, filed on 19 May 1998		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	GRANTED		
PRIMARY EXAMINER:	Cook, Rebecca		
LEGAL REPRESENTATIVE:	Oltman, Flynn & Kubler		
NUMBER OF CLAIMS:	2		
EXEMPLARY CLAIM:	1		
LINE COUNT:	282		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

(FILE 'HOME' ENTERED AT 17:05:35 ON 07 JAN 2004)

FILE 'REGISTRY' ENTERED AT 17:05:40 ON 07 JAN 2004

L1 1 S NICOTINIC ACID/CN
L2 1 S NICOTINAMIDE/CN

FILE 'CAPLUS, USPATFULL' ENTERED AT 17:06:15 ON 07 JAN 2004

L3 54239 FILE CAPLUS
L4 16273 FILE USPATFULL

TOTAL FOR ALL FILES

L5 70512 S L1 OR L2 OR NICOTINAMIDE OR NICOTINIC
L6 9 FILE CAPLUS
L7 27 FILE USPATFULL

TOTAL FOR ALL FILES

L8 36 S L5 (50A) (PRURITIS OR ITCH?)

=> d l7 1-27 hit, pi

L7 ANSWER 1 OF 27 USPATFULL on STN

DETD [0013] As regards the second effect mentioned above, niacin is used in systemic administration, i.e. by the oral or parenteral route, at higher doses than those mentioned above for the prophylaxis and treatment of pellagra (i.e. 2-6 g per day) in preparations for hyperlipidemia therapy, for lowering cholesterol levels in the blood. However, at the high systemic doses required by this treatment, both nicotinic acid and **nicotinamide** have shown a certain number of adverse side-effects, including gastrointestinal reactions (abdominal pain and nausea), hepatotoxicity and, above all, flushing (cutaneous erythema) often accompanied by warmth, tingling and **itching**.

PI US 2003181459 A1 20030925

L7 ANSWER 2 OF 27 USPATFULL on STN

SUMM **Nicotinic** acid was first reported to be hypolipidemic in 1955. Large doses (3 to 6 g/day) rapidly decrease VLDL and LDL and dramatically increase HDL even as much as 20 or 30 mg/dL. But it causes numerous side effects, most importantly an intense flushing and **pruritis**. Abnormalities of hepatic function, including jaundice, are potentially serious and can occur with 2-g day or delayed-release products. Elevated fasting glucose and delayed glucose tolerance occur frequently and rare side effects include reversible optic maculopathy, toxic amblyopia, arrhythmias, and orthostatic hypotension. See J. Hardman at pp.889-90.

PI US 6576242 B1 20030610

L7 ANSWER 3 OF 27 USPATFULL on STN

SUMM **Nicotinic** acid was first reported to be hypolipidemic in 1955. Large doses (3 to 6 g/day) rapidly decrease VLDL and LDL and dramatically increase HDL even as much as 20 or 30 mg/dL. But it causes numerous side effects, most importantly an intense flushing and **pruritis**. Abnormalities of hepatic function, including jaundice, are potentially serious and can occur with 2-g day or delayed-release products. Elevated fasting glucose and delayed glucose tolerance occur frequently and rare side effects include reversible optic maculopathy, toxic amblyopia, arrhythmias, and orthostatic hypotension. See J. Hardman at pp.889-90.

PI US 6544525 B1 20030408

L7 ANSWER 4 OF 27 USPATFULL on STN

SUMM **Nicotinic** acid was first reported to be hypolipidemic in 1955. Large doses (3 to 6 g/day) rapidly decrease VLDL and LDL and dramatically increase HDL even as much as 20 or 30 mg/dL. But it causes

numerous side effects, most importantly an intense flushing and **pruritis**. Abnormalities of hepatic function, including jaundice, are potentially serious and can occur with 2-g day or delayed-release products. Elevated fasting glucose and delayed glucose tolerance occur frequently and rare side effects include reversible optic maculopathy, toxic amblyopia, arrhythmias, and orthostatic hypotension. See J. Hardman at pp.889-90.

PI US 6541006 B1 20030401

L7 ANSWER 5 OF 27 USPATFULL on STN

SUMM **Nicotinic** acid was first reported to be hypolipidemic in 1955. Large doses (3 to 6 g/day) rapidly decrease VLDL and LDL and dramatically increase HDL even as much as 20 or 30 mg/dL. But it causes numerous side effects, most importantly an intense flushing and **pruritis**. Abnormalities of hepatic function, including jaundice, are potentially serious and can occur with 2-g day or delayed-release products. Elevated fasting glucose and delayed glucose tolerance occur frequently and rare side effects include reversible optic maculopathy, toxic amblyopia, arrhythmias, and orthostatic hypotension. See J. Hardman at pp. 889-90.

PI US 6541005 B1 20030401

L7 ANSWER 6 OF 27 USPATFULL on STN

SUMM **Nicotinic** acid was first reported to be hypolipidemic in 1955. Large doses (3 to 6 g/day) rapidly decrease VLDL and LDL and dramatically increase HDL even as much as 20 or 30 mg/dL. But it causes numerous side effects, most importantly an intense flushing and **pruritis**. Abnormalities of hepatic function, including jaundice, are potentially serious and can occur with 2-g day or delayed-release products. Elevated fasting glucose and delayed glucose tolerance occur frequently and rare side effects include reversible optic maculopathy, toxic amblyopia, arrhythmias, and orthostatic hypotension. See J. Hardman at pp.889-90.

PI US 6495173 B1 20021217

L7 ANSWER 7 OF 27 USPATFULL on STN

SUMM [0006] Another class of compounds which have been used as cholesterol-lowering agents are nicotinic acid, commonly referred to as niacin, and derivatives thereof. Niacin is a potent triglyceride reducing agent with an HDL-elevating effect. Niacin therapy is prescribed to treat patients with moderate to severe hypertriglyceridemia and does not usually produce a significant LDL cholesterol-lowering effect. Niacin acts within the liver to decrease VLDL triglyceride output and in the periphery to increase its clearance. The side effects of niacin are well-known and usually limit usage. For example, high doses cause **pruritis** and flushing. In addition, an elevation in liver enzymes, abdominal cramps, diarrhea, nausea and vomiting have been observed. Niacin is available, for example, as NICOLAR.RTM. tablets. **Nicotinic** acid derivatives include, Acipimox, Aluminum Nicotinate, Niceritrol, Nicoclonate, Nicomol and Oxiniacic Acid.

PI US 2002155091 A1 20021024

L7 ANSWER 8 OF 27 USPATFULL on STN

SUMM **Nicotinic** acid was first reported to be hypolipidemic in 1955. Large doses (3 to 6 g/day) rapidly decrease VLDL and LDL and dramatically increase HDL even as much as 20 or 30 mg/dL. But it causes numerous side effects, most importantly an intense flushing and **pruritis**. Abnormalities of hepatic function, including jaundice, are potentially serious and can occur with 2-g day or delayed-release

products. Elevated fasting glucose and delayed glucose tolerance occur frequently and rare side effects include reversible optic maculopathy, toxic amblyopia, arrhythmias, and orthostatic hypotension. See J. Hardman at pp.889-90.

PI US 6436406 B1 20020820

L7 ANSWER 9 OF 27 USPATFULL on STN

SUMM [0010] Known pharmaceutical agents for treating hypertriglyceridemia include the class of fibrate drugs, e.g., clofibrate, benzafibrate and gemfibrozil, as well as **nicotinic** acid and derivatives thereof. **Nicotinic** acid has been shown to be safe and effective for lowering serum TG levels, but the therapeutic dosage must be worked up to gradually to minimize the flushing and **itching** of skin which frequently cannot be tolerated by the patient. Clinically relevant interactions of fibrates with other anti-hyperlipidemic drugs include rhabdomyolysis when used in combination with HMG CoA-reductase inhibitors (statins), and decreased bioavailability when combined with certain bile acid sequesterants (Farmer and Gotto, 1994). Also, potentiation of the anticoagulant effects of coumarin may cause bleeding (Blum, 1992).

PI US 2002044981 A1 20020418
US 6667064 B2 20031223

L7 ANSWER 10 OF 27 USPATFULL on STN

SUMM Another class of compounds which have been used as cholesterol-lowering agents are nicotinic acid, commonly referred to as niacin, and derivatives thereof. Niacin is a potent triglyceride reducing agent with an HDL-elevating effect. Niacin therapy is prescribed to treat patients with moderate to severe hypertriglyceridemia and does not usually produce a significant LDL cholesterol-lowering effect. Niacin acts within the liver to decrease VLDL triglyceride output and in the periphery to increase its clearance. The side effects of niacin are well-known and usually limit usage. For example, high doses cause **pruritis** and flushing. In addition, an elevation in liver enzymes, abdominal cramps, diarrhea, nausea and vomiting have been observed. Niacin is available, for example, as NICOLAR.RTM. tablets. **Nicotinic** acid derivatives include, Acipimox, Aluminum Nicotinate, Niceritol, Nicoclonate, Nicomol and Oxiniacic Acid.

PI US 6365186 B1 20020402

L7 ANSWER 11 OF 27 USPATFULL on STN

SUMM The active compounds of the present invention have antimicrobial (e.g., antibacterial and antifungal) activity These compounds are useful for the treatment of conditions including, but not limited to, acne vulgaris, preadolescent acne, rosacea, premenstrual acne, acne venenata, acne cosmetica, pomade acne, acne detergicans, acne cosmetica, acne excorie, gram negative acne, steroid acne, acne conglobata, or nodulocystic acne. The present invention can also be used for topically treating certain types of dermatitis, e.g. perioral dermatitis, seborrheic dermatitis, gram negative folliculitis, sebaceous gland dysfunction, hidradenitis suppurativa, pseudofolliculitis barbae, folliculitis and derratophyte infections (e.g., such as ringworm, athletes foot, and jock **itch**). The compounds are also useful in methods of preventing or ameliorating undesirable body odor. Sclareolide-like compounds (in particular, sclareolide) evaluated using the techniques described in Bencherif et al., JPET 279, 1413-1421 (1996) are determined to exhibit a profile for inhibition of human **nicotinic** receptor function similar to forskolin (which is well established as an activator of adenylyl cyclase).

PI US 6331551 B1 20011218

L7 ANSWER 12 OF 27 USPATFULL on STN

SUMM [0006] Oral niacin therapy has side effects that limit its utility. Although niacin is a vitamin, it must be used in therapeutic doses to lower cholesterol. At these doses, both immediate-release and sustained-release niacin can have several side effects. The most common side effect of niacin is flushing, a warm feeling in the skin usually associated with redness and sometimes **itching**. Flushing is not dangerous but most patients find it very uncomfortable, which seriously limits patient compliance with therapy. Niacin-induced flushing can be substantially attenuated by pretreatment with cyclooxygenase inhibitors, suggesting that the vasodilation is caused by a prostaglandin-mediated mechanism (see Carlson, L. A., **Nicotinic** acid and inhibition of fat mobilizing lipolysis. Present status, of effects on lipid metabolism, Adv Exp Med Biol 109: 225-238, 1978).

PI US 2001049382 A1 20011206

L7 ANSWER 13 OF 27 USPATFULL on STN

AB Compositions for skin treatment are disclosed and include **nicotinamide**, **nicotinic** acid, and **nicotinic** esters as active ingredients. The compositions are applied topically to the skin to treat skin conditions including acne, fine lines and age spots, **itching** and pain from insect bites, bee stings, fungi (including athletes foot and jock **itch**), flaking and/or scaly skin (including dandruff, seborrheic dermatitis, psoriasis and heat rash), and burns. Different compositions are presented for use as an acne treatment, a face and body wash, a dermatophyte (nail fungus) treatment. Still another is intended for use in makeup, and another in lipstick.

SUMM The present invention relates to a discovery that a nicotinic ester and particularly the compound methyl nicotinate, is highly beneficial when topically applied to treat skin conditions. More particularly, when combined with a skin moisturizer, a suitable carrier, an emollient (e.g. glycerol or glycerin), vitamin E and other elements and excipients, methyl nicotinate, and **nicotinic** acid have surprising efficacy in treating various skin conditions including: acne blemishes; acne pimples, blackheads and whiteheads; psoriasis; seborrheic dermatitis, or dandruff; large pores, fine lines and age spots; stretch marks; cellulite; **itching**; pain and **itching** from insect bites and stings; fungi; varicose veins; flaking and scaly skin; burns (including sunburn); bedsores and black and blue marks.

PI US 6248763 B1 20010619

L7 ANSWER 14 OF 27 USPATFULL on STN

SUMM The active compounds of the present invention have antimicrobial (e.g., antibacterial and antifungal) activity. These compounds are useful for the treatment of conditions including, but not limited to, acne vulgaris, preadolescent acne, rosacea, premenstrual acne, acne venenata, acne cosmetica, pomade acne, acne detergentica, acne cosmetica, acne excorie, gram negative acne, steroid acne, acne conglobata, or nodulocystic acne. The present invention can also be used for topically treating certain types of dermatitis, e. g. perioral dermatitis, seborrheic dermatitis, gram negative folliculitis, sebaceous gland dysfunction, hidradenitis suppurativa, pseudofolliculitis barbae, folliculitis and dermatophyte infections (e.g., such as ringworm, athletes foot, and jock **itch**). The compounds are also useful in methods of preventing or ameliorating undesirable body odor. Sclareolide-like compounds (in particular, sclareolide) evaluated using the techniques described in Bencherif et al., JPET 279, 1413-1421 (1996) are determined to exhibit a profile for inhibition of human **nicotinic** receptor function similar to forskolin (which is well established as an activator of adenylyl cyclase).

PI US 6150381 20001121

L7 ANSWER 15 OF 27 USPATFULL on STN

SUMM However, the doses required to lower atherogenic serum lipids are quite large, on the order of 1-8 grams per day. At these levels, adverse side effects are frequent, and may include gastrointestinal disturbances such as nausea, heartburn, and diarrhea. However, the most frequent and prominent side effect is intense flushing, often accompanied by cutaneous **itching**, tingling, or warmth, and occasionally by headache. Although the flushing side effect is in general harmless, it is sufficiently unpleasant that patient compliance is markedly reduced. Often, 30-40% of patients cease taking **nicotinic** acid within days after initiating therapy. Consequently, significant efforts have been exerted to develop niacin analogs, dosage forms, and treatment protocols which minimize the flush reaction.

PI US 5981555 19991109

L7 ANSWER 16 OF 27 USPATFULL on STN

SUMM On the other hand, as the medicines to lower both a cholesterol level and a triglyceride level, there have been put into practical use clofibrate type medicines and pharmaceutical preparations of **nicotinic** acid; however, **nicotinic** acid may develop at a high frequency side-effects such as **itching**, feverish feeling, rash etc., while clofibrate type medicines have presented the problem of side-effects such as easier formation of gallstone, muscular disorders, hepatic dysfunctions, gastrointestinal disorders, etc. There has been also presented the problem of a considerably higher dose, a dose of niacin as a pharmaceutical preparation of **nicotinic** acid being 2-3 g and aluminum clofibrate being 1.5 g.

PI US 5801143 19980901
WO 9532990 19951207

L7 ANSWER 17 OF 27 USPATFULL on STN

SUMM The ability of large doses of **nicotinic** acid (i.e., niacin) to lower serum lipid levels has been recognized for many years. This drug is unusually effective because it lowers the levels of several classes of morbidity-associated serum lipids, including LDL cholesterol (LDL-C), Lp(a), and triglycerides (Tg). In addition to its antilipemic activity, niacin is also an essential water-soluble vitamin. **Nicotinic** acid exhibits relatively low toxicity on a molar basis. However, the doses required to lower atherogenic serum lipids are quite large, on the order of 1-8 grams per day. At these levels, adverse side effects are frequent, and may include gastrointestinal disturbances such as nausea, heartburn, and diarrhea. However, the most frequent and prominent side effect is intense flushing, often accompanied by cutaneous **itching**, tingling, or warmth, and occasionally by headache. Although the flushing side effect is in general harmless, it is sufficiently unpleasant that patient compliance is markedly reduced. Often, 30-40% of patients cease taking **nicotinic** acid within days after initiating therapy. Consequently, significant efforts have been exerted to develop niacin analogs, dosage forms, and treatment protocols which minimize the flush reaction.

PI US 5773453 19980630

L7 ANSWER 18 OF 27 USPATFULL on STN

SUMM The known drugs that may be used to reduce the quantity of lipids in blood serum are: **nicotinic** acid and its derivatives, cholesterol synthesis inhibitors, Probucol and so forth. Also, water-soluble dietary fibers such as vegetable gums, including pectin, are food constituents that are known to have the effect of improving

lipid metabolism. However, adverse side effects such as hot flashes, **itchiness**, and muscular impairment have been reported when the above mentioned antihyperlipidemics are used, and they have not yet been proved to be safe. Moreover, for an adult to obtain an appreciable lipid lowering effect or a significant improvement in lipid metabolism, the water-soluble dietary fibers mentioned above, such as vegetable gums, including pectin, must be taken in quantities of 10 grams to several tens of grams per day. It is extremely difficult to take a solution of vegetable gum such as pectin in such great quantities, however, because of its high viscosity. In practice, therefore, it is almost impossible to take dietary fibers in aqueous solution in sufficient quantities on a daily basis.

PI US 5527784 19960618

L7 ANSWER 19 OF 27 USPATFULL on STN

DETD In accordance with the present invention, the nicotinic acid (also called niacin) may be formulated as tablets, capsules or powder preparations, each having a measured unit of administration of about 25-100 mg. Preferably, the nicotinic acid is limited to about 100 mg per dosage since oral administration of this odorless, crystalline compound in amounts substantially greater than 100 mg per dose can result in a physiological reaction referred to as the "niacin flush". This reaction is believed to be caused by the vasodilator and histamine-releasing effects of **nicotinic** acid, and is generally experienced as tingling or **itching** sensation, which may be accompanied by reddening in of the face and other parts of the body. These symptoms may persist for 20-30 minutes, but usually diminish and completely disappear with continued administration of niacin at dosage levels of 100 mg, taken three times per day at morning, noon and evening. While individual sensitivity to niacin varies, it may be may be advisable for certain hypersensitive patients to use 1/2 or 1/4 of a scored 100 mg niacin tablet for at least one week at the beginning of the present therapy. Thereafter, if no significant discomfort or flushing is observed. nicotinic acid may be continued at the preferred maintenance dose of 100--mg three times/day indefinitely.

PI US 5358720 19941025

L7 ANSWER 20 OF 27 USPATFULL on STN

SUMM Hypercholesterolemia, particularly increased low density lipoproteinemia-cholesterol (LDL) and hypertriglyceridemia, associated with particularly very low density lipoproteinemia-cholesterol (VLDL), may coexist in the atherosclerotic patient or may exist separately. Likewise, some forms of therapy are better suited to reduction of one or another type of hyperlipidemia. For instance, the bile acid sequestrants, such as cholestyramine and cholestipol decrease LDL cholesterol but are not effective in lowering triglyceridemia. The dosage of 4 or 5 grams taken as a suspension orally twice a day limits their acceptance by the patient. **Nicotinic** acid is effective and safe for lowering particularly triglyceridemia, but the dosage of 1.5 to 3 grams/day must be worked up to gradually to minimize the flushing and **itching** of skin which frequently cannot be tolerated by the patient.

PI US 5110817 19920505

L7 ANSWER 21 OF 27 USPATFULL on STN

DETD The results of these Experimental Examples 1 to 4 indicate that the compounds of the present invention sustain an excellent antihyperlipemic effect of **nicotinic** acid while relieving the side effects thereof, for example, rubor or **itching**, by slowly releasing **nicotinic** acid. Since vitamin E is effective in lowering lipid level, the compounds of the present invention are useful as a remedy for arteriosclerosis which sustains the basic pharmacological effects of

both of vitamin E and **nicotinic** acid, namely, improving circulation and lipid metabolism, while relieving the side effects of nicotinic acid.

PI US 5102895 19920407

L7 ANSWER 22 OF 27 USPATFULL on STN

SUMM The prior art is replete with reports of the reduction of cholesterol levels and control of cholesterol levels in a subject in need of the same employing niacin (**nicotinic** acid) and of the undesirable side effects ordinarily produced when an effective amount of niacin is employed for such purpose. The side effects include flushing and **itching**, and it is well documented in the literature that such flushing, **itching**, and so on is not eliminated by intermittent niacin therapy, and generally reappears even when the therapy is interrupted and reinstituted. Although the degree or intensity of such side effects varies from patient to patient, it is frequently observed that such therapy cannot be applied in the case of various patients who are hypersensitive to the niacin or to the side effects which result in such patients upon oral administration thereof.

DETD According to the practice of the art, the niacin or nicotinic acid may be provided as such or in the form of a prodrug thereof, numerous of which are presently available and which break down, to a greater or lesser extent upon ingestion, to provide nicotinic acid in the system of the subject orally ingesting the same for reduction or control of cholesterol levels in the said subject. Representative prodrugs of this type are derivatives of **nicotinic** acid, especially esters, and the like, and many of these prodrugs are also subject to the same side effects as niacin itself, namely, the production of the undesirable and sometimes intolerable side effects of flushing, **itching**, and the like and, to the extent that these prodrugs do provide an effective antihyperlipidemic amount of **nicotinic** acid upon ingestion, as well as the undesirable side effects of niacin previously mentioned, they may be employed according to the present invention in lieu of niacin itself, the method and combination compositions of the present invention providing effective cholesterol-lowering effect as well as reduction or essential elimination of the undesirable effects of niacin when such a prodrug is employed just as in the case of the employment of niacin itself.

DETD It is therefore seen that the present invention provides an oral antihyperlipidemic composition of **nicotinic** acid (niacin) characterized by reduced and related flushing effects comprising as active ingredients **nicotinic** acid and guar gum or another gel-forming dietary fiber, which is effective in lowering of cholesterol levels, especially LDL cholesterol levels, without the usual undesirable flushing, **itching**, and related side effects of niacin, and a method of lowering cholesterol levels by employment of such an oral pharmaceutical or dietary supplement composition, or by the simultaneous oral administration of the active ingredients thereof, all having the unpredictable and highly advantageous characteristics and effects as more fully set forth in the foregoing.

PI US 5023245 19910611

L7 ANSWER 23 OF 27 USPATFULL on STN

SUMM The prior art is replete with reports of the reduction of cholesterol levels and control of cholesterol levels in a subject in need of the same employing niacin (**nicotinic** acid) and of the undesirable side effects ordinarily produced when an effective amount of niacin is employed for such purpose. The side effects include flushing and **itching**, and it is well documented in the literature that such flushing, **itching**, and so on is not eliminated by intermittent niacin therapy, and generally reappears even when the therapy is interrupted and reinstituted. Although the degree or intensity of such side effects varies from patient to patient, it is frequently observed

that such therapy cannot be applied in the case of various patients who are hypersensitive to the niacin or to the side effects which result in such patients upon oral administration thereof.

DETD According to the practice of the art, the niacin or nicotinic acid may be provided as such or in the form of a prodrug thereof, numerous of which are presently available and which break down, to a greater or lesser extent upon ingestion, to provide nicotinic acid in the system of the subject orally ingesting the same for reduction or control of cholesterol levels in the said subject. Representative prodrugs of this type are derivatives of **nicotinic** acid, especially esters, and the like, and many of these prodrugs are also subject to the same side effects as niacin itself, namely, the production of the undesirable and sometimes intolerable side effects of flushing, **itching**, and the like and, to the extent that these prodrugs do provide an effective antihyperlipidemic amount of nicotinic acid upon ingestion, as well as the undesirable side effects of niacin previously mentioned, they may be employed according to the present invention in lieu of niacin itself, the method and combination compositions of the present invention providing effective cholesterol-lowering effect as well as reduction or essential elimination of the undesirable effects of niacin when such a prodrug is employed just as in the case of the employment of niacin itself.

DETD It is therefore seen that the present invention provides an oral antihyperlipidemic composition of **nicotinic** acid (niacin) characterized by reduced and related flushing effects comprising as active ingredients **nicotinic** acid and guar gum, which is effective in lowering of cholesterol levels, especially LDL cholesterol levels, without the usual undesirable flushing, **itching**, and related side effects of niacin, and a method of lowering cholesterol levels by employment of such an oral pharmaceutical or dietary supplement composition, or by the simultaneous oral administration of the active ingredients thereof, all having the unpredictable and highly advantageous characteristics and effects as more fully set forth in the foregoing.

PI US 4965252 19901023

L7 ANSWER 24 OF 27 USPATFULL on STN

SUMM Hypercholesterolemia, particularly increased low density lipoproteinemia-cholesterol (LDL) and hypertriglyceridemia, associated with particularly very low density lipoproteinemia-cholesterol (VLDL), may coexist in the atherosclerotic patient or may exist separately. Likewise, some forms of therapy are better suited to reduction of one or another type of hyperlipidemia. For instance, the bile acid sequestrants, such as cholestyramine and cholestipol decrease LDL cholesterol but are not effective in lowering triglyceridemia. The dosage of 4 or 5 grams taken as a suspension orally twice a day limits their acceptance by the patient. **Nicotinic** acid is effective and safe for lowering particularly triglyceridemia, but the dosage of 1.5 to 3 grams/day must be worked up to gradually to minimize the flushing and **itching** of skin which frequently cannot be tolerated by the patient.

PI US 4920123 19900424

L7 ANSWER 25 OF 27 USPATFULL on STN

SUMM The prior art is replete with reports of the reduction of cholesterol levels and control of cholesterol levels in a subject in need of the same employing niacin (**nicotinic** acid) and of the undesirable side effects ordinarily produced when an effective amount of niacin is employed for such purpose. The side effects include flushing and **itching**, and it is well documented in the literature that such flushing, **itching**, and so on is not eliminated by intermittent niacin therapy, and generally reappears even when the therapy is

interrupted and reinstituted. Although the degree or intensity of such side effects varies from patient to patient, it is frequently observed that such therapy cannot be applied in the case of various patients who are hypersensitive to the niacin or to the side effects which result in such patients upon oral administration thereof.

DETD According to the practice of the art, the niacin or nicotinic acid may be provided as such or in the form of a prodrug thereof, numerous of which are presently available and which break down, to a greater or lesser extent upon ingestion, to provide nicotinic acid in the system of the subject orally ingesting the same for reduction or control of cholesterol levels in the said subject. Representative prodrugs of this type are derivatives of **nicotinic** acid, especially esters, amides, and the like, and many of these prodrugs are also subject to the same side effects as niacin itself, namely, the production of the undesirable and sometimes intolerable side effects of flushing, **itching**, and the like and, to the extent that these prodrugs do provide **nicotinic** acid upon ingestion, as well as the undesirable side effects of niacin previously mentioned, they may be employed according to the present invention in lieu of niacin itself, the method and combination compositions of the present invention providing effective cholesterol-lowering effect as well as reduction or essential elimination of the undesirable effects of niacin when such a prodrug is employed just as in the case of the employment of niacin itself.

PI US 4911917 19900327

L7 ANSWER 26 OF 27 USPATFULL on STN

DETD It is well known that nicotinic acid has a vasodilator effect and reduces the levels of lipids such as cholesterol, triglycerides, phospholipids and free fatty acids in blood. However, **nicotinic** acid has some adverse and undesirable effects when used in clinical treatment. For instance, the **nicotinic** acid level in the blood rapidly decreases when administered at normal dosage levels while, at higher doses, it causes various side-effects such as flushing of the face, **itching** and gastrointestinal impediments. Some of the side effects are caused by the rebound phenomenon which is, that after administration of **nicotinic** acid, the blood **nicotinic** acid level rapidly reaches a maximum level and then decreases in a short time.

PI US 4288441 19810908

L7 ANSWER 27 OF 27 USPATFULL on STN

SUMM It is known that cholesterol and triglyceride levels in plasma can be decreased by the use of **nicotinic** acid [Clin. Med. 82 (7), 19-26(1975); Atherosclerosis 18(1), 1- 9(1973)]. However, the use of **nicotinic** acid as a hypolipidemic agent possesses undesirable side effects such as facial skin flush and **itching**. On the other hand, carnitine, normally present in the body, enzymatically combines with fatty acids to facilitate their transport through the mitochondrial membranes and is an important factor in metabolism of fatty acids [Pharmacological Society 56(6), page 798(1970)]. In this connection, Japanese patent application No. 530044/1973(laid open to the public without examination under No. 47519/1974) discloses that carnitine, when used in combination with a lipolytic agent, is useful in treating the obesity of mammals. Additionally, the synthesis of several carnitine esters has been reported recently. For example, the synthesis of carnitine alkyl esters, O-linoleyl carnitine chloride and carnitine, have been disclosed in Chemical Abstracts 64(1966), 19398g, Japanese patent publication No. 24006/1972 and Japanese patent publication No. 24/1963, respectively.

SUMM During the course of various investigations, we have now succeeded in the synthesis of a novel carnitine ester, i.e., O-nicotioyl carnitine

compound, and at the same time found that it is useful as a hypolipidemic agent. The nicotinoyl carnitine compound [I] of the present invention exhibits a potent hypotriglyceridemic and hypocholesterolemic activity, and the activity of the compound [I] lasts longer than that of **nicotinic** acid. Further, it has a remarkably low toxicity and does not show side effects such as facial skin flushing, **itching**, etc. to any substantial degree. The nicotinoyl carnitine derivative [I] may be therefore useful in treating or preventing arteriosclerosis, cardiac infarction, stenocardia, cerebral hemorrhage, softening of the brain, hypercholesteremia and/or lipemia.

PI US 4032641 19770628

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L7 ANSWER 13 OF 27 USPATFULL on STN

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REMARKS:		
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